REMARKS

Reconsideration of this application pursuant to applicants' request for continued examination is requested.

Claim 1 has been amended to indicate that the library comprises approximately 10^7 individual members based on the applicants' disclosure at page 12, lines 9-13. This provides a library having a very high level of complexity. This high level of complexity may be accomplished in the manner described in applicants' Example 1 by using at least two different restriction sites. While the applicants do not agree with the Examiner's view that U.S. 5,800,988 and EP 584421 disclose the use of nucleic acid sequences cloned from a non-immunized source, the issue becomes moot in view of the aforementioned amendment of claim 1. Clearly, there is no disclosure or suggestion in U.S. Patent 5,800,988 or EP 584421 to provide a library possessing the high level of complexity called for in the applicants' claims.

In particular, there is nothing in either reference disclosing or suggesting a library as claimed wherein the library comprises at least or approximately 10^7 individual members with a very high level of complexity. Accordingly, regardless of the Examiner's position as to whether or not the source of the nucleic acid sequences in the reference is non-immunized or immunized, the applicants' claims distinguish patentably over the references in view of the clearcut novelty in the very high level of complexity offered by the applicants' library. Accordingly, it is urged that the Section 102(a) rejection of applicants' claims based on Casterman U.S. 5,800,988 and the companion Section 102(b) rejection based on Casterman EP 584421 should be withdrawn.

In connection with the foregoing, it is to be noted that in applicants' specification (page 14, beginning at line 8), it is disclosed that a second series of PCR products was obtained introducing a second type of restriction site (SfiI), since the PstI restriction site in the first primer would theoretically also be present in 10% of the amplified fragments. Thus, to achieve a high level of complexity, the applicants used a combination of PCR primers with at least two different restriction sites so that no fragments were lost during the cloning process. Casterman does not suggest using more than one primer to avoid internal restriction sites. In the circumstances, it is considered that Casterman's process would not enable or suggest obtaining the high level of diversity obtained by the applicants' invention.

For basically similar reasons, the applicants submit that the Examiner should withdraw the Section 102(b)/103(a) rejection of applicants' claims based on Ghahroudi et al. This reference does not disclose or suggest the applicants' library as claimed with the very high level of complexity resulting, in large part, from the applicants' use of nucleic acid sequences cloned

from a non-immunized source and with the other characteristics called for by the applicants. It is not considered appropriate for the Examiner to disregard the applicants' claim limitation "cloned from a non-immunized source" as, in essence, a non-substantive process feature. There are fundamental differences between nucleic acid sequences which are cloned from an immunized source and those cloned from a non-immunized source. More particularly, because of the immunization reaction, the libraries according to Ghahroudi will be enriched in antibodies that bind to the antigen that was used for immunization. The applicants' libraries are not enriched with one specific family of antibodies but contain the antibody variety that is present in the non-immunized source. As a consequence, the applicants' libraries have a very high level of complexity. As applicants have previously pointed out, it is surprising that this diversity is obtained in the absence of light chains because this theoretically creates a lower diversity in the library.

Favorable reconsideration and allowance of this application are requested.

Respectfully submitted,

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